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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,608	12/12/2003	Marcel P. Bruchez	IVGN 620.2 CIP	1956
23358	7590	08/22/2007	EXAMINER	
INVITROGEN CORPORATION			JUNG, UNSU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,608	BRUCHEZ ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,6,7,10-13 and 16-43 is/are pending in the application.
- 4a) Of the above claim(s) 17-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,6,7,10-13,16 and 38-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/30/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The Examiner for the current application has been changed from Pensee Do to Unsu Jung in Art Unit 1641. Any inquiry concerning this application should be directed to Unsu Jung, whose contact information is provided in the conclusion section of this Office Action.

2. Applicant's reply filed on May 30, 2007 has been acknowledged and entered. The reply included amendments to claims 1, 3, 6, 10, 12, 16, and 40, cancellation of claim 5, 8, 9, 14, and 15, and addition of new claims 42 and 43.

It has been further noted that status identifier for claim 1 is incorrectly labeled as "previously presented." Claim 1 has been amended to include the limitation of "core surrounded by a semiconductor shell, and wherein the cationic polymer consists of 5 to 25 contiguous Lys and/or Arg residues. The status identifier should reflect the current status of the claim 1, i.e. "Currently Amended."

3. Claims 1, 3, 4, 6, 7, 10-13, and 16-43 are pending, claims 17-37 have been withdrawn from consideration, and claims 1, 3, 4, 6, 7, 10-13, 16, and 38-43 are under consideration for their merits.

Information Disclosure Statement

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4. The information disclosure statement (IDS) submitted on May 30, 2007 has been considered by the examiner. Further, relevant page numbers (pp410-417) for citation No. C6 has been included as indicated on the IDS.

Rejections Withdrawn

5. Upon further consideration, the following rejections have been withdrawn in view of amended independent claim 1 in the reply filed on May 30, 2007:

- Rejection of claims 1, 3-4 under 35 U.S.C. 102(e) as being anticipated by Jacobson et al. (U.S. Patent No. 6,953,656, filed on July 14, 2000);
- Rejection of claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Jacobson et al. in view of Bawendi (U.S. Patent No. 6,306,610, filed on Sept. 17, 1999);
- Rejection of claims 1, 3-7, 11-13, 38 and 39 under 35 U.S.C. 103(a) as being unpatentable over admitted prior art in the present specification in view of Bawendi; and
- Rejection of claims 8-10, 14-16, 40 and 41 under 35 U.S.C. 103(a) as being unpatentable over admitted prior art in the present specification in view of Bawendi, and further in view of Frankel (U.S. Patent No. 5,652,122, July 29, 1997).

A typo has been noted in the Office Action dated January 30, 2007 on p5, 2nd paragraph, where the U.S. Patent No. for Frankel reference has been incorrectly

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indicated as being "5,652,152." The U.S. Patent No. for Frankel reference should be corrected to 5,652,122.

Specification

6. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected. Appropriate corrections are required.

Trademarks (For example, Cascade Blue[®], BODIPY[™], CY[®], Texas Red[®], and others listed in Table 1, on pp26-30) should be capitalized or accompanied by the [®] or [™] symbol wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3, 4, 6, 7, 10, 11, 38, 40, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a

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way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A. Claims 1, 3, 4, 6, 7, 10, 11, 38, and 40

The specification as originally filed does not provide support for the invention as now claimed: semiconductor nanoparticle complex of claim 1 and all dependent claims thereof includes “a cationic polymer consisting of 5 to 25 contiguous Lys and/or Arg residues”.

Applicant’s amendment filed on May 30, 2007 directs support to 20-22 (paragraphs 206-228) of the specification.

Although, the specification discloses a cationic polymer containing/having 4 to 25 contiguous Lys or Arg (p55, lines 16-26) and the original claims 10 and 16 recites a cationic polymer containing/having 5 to 25 contiguous Lys and/or Arg, the specification fails to disclose “a cationic polymer consisting of 5 to 25 contiguous Lys and/or Arg residues.” According to MPEP 2111.01, transitional phrases such as “comprising,” “having,” and “containing” are inclusive or open-ended and do not exclude additional, unrecited elements, while “consisting” is a closed term and does exclude additional, unrecited elements. Therefore, the scope of the invention as now claimed is not supported by the as-filed specification.

In addition, adding the expressed exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This

clearly illustrates that such negative limitations do, in fact, introduce new concepts. See *Ex parte Grasselli*, 231 USPQ 393 (BPAI 1983).

The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

B. Claims 42 and 43

The specification as originally filed does not provide support for the invention as now claimed: semiconductor nanoparticle complex of claims 42 and 43 includes a limitation "wherein a cationic polymer is not a tat peptide".

Applicant's amendment filed on May 30, 2007 directs support to 20-22 (paragraphs 206-228) of the specification. However, support for the limitation of new claims 42 and 43, "wherein a cationic polymer is not a tat peptide" is not found in the as-filed specification.

In addition, the recitation of "wherein a cationic polymer is not a tat peptide" appears to be a negative limitation. Adding the expressed exclusion of certain elements implies the permissible inclusion of all other elements not so expressly

excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts. See *Ex parte Grasselli*, 231 USPQ 393 (BPAI 1983).

The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action.

Alternatively, applicant is invited to provide sufficient written support for the limitations "cationic polymer consisting of 5 to 25 contiguous Lys and/or Arg residues" and "wherein a cationic polymer is not a tat peptide" indicated above.

See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 3, 4, 6, 7, 10-13, 16, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (*Science*, 1998, Vol. 281, pp2016-2018) in view of Rothbard et al. (U.S. Patent No. 6,495,663, filed on May 21, 1998).

According to the specification on p14, lines 25-30, the terms "semiconductor nanocrystal," "quantum dot" and "Qdot™ nanocrystal" are used interchangeably herein to refer to semiconductor nanoparticles composed of an inorganic crystalline material that is luminescent (i.e., they are capable of emitting electromagnetic radiation upon excitation), and include an inner core of one or more first semiconductor materials that is optionally contained within an overcoating or "shell" of a second semiconductor material.

Chan et al. teaches highly luminescent semiconductor quantum dots (semiconductor nanoparticles), which are biocompatible and are suitable for use in cell biology and immunoassays (see entire document, particularly Abstract). The advantages of using semiconductor quantum dots/ nanoparticles over the conventional organic fluorescent dyes are well known in the art. The advantages include resistance to photobleaching and enhanced quantum yield (p2017, Fig. 3 and 3rd column). The improved photostability of the semiconductor quantum dots/ nanoparticles would allow real-time observations of molecular trafficking in living cells (p2017, 2nd column, last paragraph). Further, sufficiently monodispersed semiconductor quantum dots/ nanoparticles would allow use in multiplex detection schemes (p2017, 2nd column, last paragraph).

With respect to claims 3 and 4, Chan et al. teaches a semiconductor nanoparticles comprising CdSe core (Fig. 1).

With respect to claims 6 and 7, Chan et al. teaches a semiconductor nanoparticles comprising ZnS shell (Fig. 1).

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With respect to claims 12 and 13, Chan et al. teaches a semiconductor nanoparticles comprising CdSe core and ZnS shell (Fig. 1).

However, Chan et al. fails to specifically teach a semiconductor nanoparticle complex, wherein the semiconductor nanoparticle is bound to a cationic polymer consisting of 5 to 25 contiguous Lysine (Lys) and/or Arginine (Arg) residues.

Rothbard et al. teaches methods and composition for transporting drugs and macromolecules across biological membranes wherein the biological membranes are contacted with a conjugate containing a biologically active agent that is covalently attached to a transport polymer (translocatable molecule, see entire document). Such transport polymer has 5 to 25 subunits of Lys or Arg (SEQ ID NO's 2, 3-11 and 13-17). The transport enhancing polymers are exemplified by peptides in which Lys or Arg residues constitute the subunits (SEQ ID NO's 2, 3-11 and 13-17). Exemplary eukaryotic cell membranes of interest include membranes of dendritic cells, epithelial cells, endothelial cells, keratinocytes, muscle cells, fungal cells, bacterial cells, plant cells and the like (column 3, lines 17-25). The conjugate is effective to enhance the transport rate of the conjugate across the biological membrane relative to the transport rate of the non-conjugate macromolecules along (column 6, line 63-column 7, line 5). Detecting uptake of macromolecules may be facilitated by attaching a fluorescent tag (see column 11, lines 3-4). Fluorescently labeled peptide polymers composed of 6 or more Arginine residues entered cells more efficiently than the tat sequence 49-57 in Fig. 1 (see column 11, lines 30-40).

With respect to claim 10, Rothbard et al. teaches a cationic polymer having 9 Arg residues (SEQ ID NO: 17).

With respect to claim 11, Rothbard et al. teaches a cationic polymer capable of enhancing the transport across a cell membrane (column 3, lines 17-25 and column 6, line 63-column 7, line 5).

With respect to claim 16, Rothbard et al. teaches a cationic polymer consisting of 6 to 25 contiguous Lys or Arg residues (SEQ ID NO:'s 2, 3-11 and 13-17).

With respect to claims 42 and 43, Rothbard et al. teaches a cationic polymer, which is not a tat peptide, comprising 5 to 25 contiguous Lys and/or Arg residues (SEQ ID NO:'s 1-17).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ a cationic polymer consisting of 5 to 25 contiguous Lys or Arg as taught by Rothbard et al. coupled to the semiconductor nanoparticles of Chan et al. in order to transport the semiconductor nanoparticle complex across the biological membrane. The advantage of using cationic polymer, which enhances the transport rate of the semiconductor nanoparticle complex across the biological membrane, provides the motivation to combine teachings of Chan et al. and Rothbard et al. since Chan et al. teaches cell-labeling using semiconductor nanoparticles via receptor-mediated endocytosis (p2018, 1st column) and Rothbard's use of the cationic polymer would facilitate transport across the cell membrane in the endocytosis taught by Chan et al. Further, one of ordinary skill in the art would have had a reasonable expectation of success in employing a cationic polymer consisting of 5 to 25 contiguous Lys or Arg as

taught by Rothbard et al. coupled to the semiconductor nanoparticles of Chan et al. since Rothbard et al. teaches that cationic polymer consisting of 5 to 25 contiguous Lys or Arg can be used for transport of conjugates across the biological membrane of eukaryotic and prokaryotic cells.

13. Claims 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (*Science*, 1998, Vol. 281, pp2016-2018) in view of Rothbard et al. (U.S. Patent No. 6,495,663, filed on May 21, 1998) as applied to claims 1, 10, 12, and 16 above, and further in view of Foster et al. (U.S. Patent No. 4,444,879, Apr. 24, 1984) and Boguslaski et al. (U.S. Patent No. 5,420,016, May 30, 1995).

Chan et al. in view of Rothbard et al. teaches a semiconductor nanoparticle complex as set forth in item 12 above. However, Chan et al. in view of Rothbard et al. fails to teach that the semiconductor nanoparticle complex is in a kit with instructions for using the semiconductor nanoparticle complex.

Foster et al. teaches a kit comprising reagents for performing an assay and instructions for providing procedure for the use of the kit (see entire document, particularly column 15, lines 30-34).

Boguslaski et al. teaches that a test kit assembled by various system components for conducting assays is more convenient and facile for the test operator (see entire document, particularly column 7, lines 8-11).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to assemble the components of Chan et al. with instructions for

providing procedure for the use of the kit as taught by Foster et al. in order to provide reagents in an assembled components for conducting various assays. The advantage of assembling reagents in a kit, which makes its use more convenient and facile for a test operator as taught by Boguslaski et al. provides the motivation to combine teachings of Chan et al. and Foster et al. with a reasonable expectation of success. In addition, the advantage of giving instructions for performing the assay for the user provides the motivation for including instructions of Foster et al. in the composition of Chan et al. with a reasonable expectation of success as the instructions would provide guidelines of how the assay should be performed for the user.

Conclusion

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Unsu Jung/
Unsu Jung, Ph.D.
Patent Examiner


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